Anticancer, Inc. v. Fujifilm Medical Systems U.S.A., Inc., et al
U.S. District Court Case No. 09CV01311-WQH (JMA)

Joint Claim Construction Chart
February 7, 2011

U.S. Patent No. 6,649,159

Claim Language: '159 Patent	Agreed Proposed Claim Construction	AntiCancer's Proposed Construction	Defendants' Proposed Construction
1. A method to monitor the ability of a promoter to promote expression in an animal of an endogenous gene that is controlled by said promoter, which method comprises:	**"Promoter"**: A genetic segment which controls the expression of the gene to which it is linked (i.e., it acts as the "on/off switch") for the expression of that gene	**A method to monitor the ability of a promoter to promote expression in an animal of an endogenous gene that is controlled by said promoter:** a method to study when a promoter (defined below) is active in an animal so that its associated endogenous gene (defined below) produces a protein, which includes the following steps. Support in Specification '159, Col. 2, ll. 58-64 '159, Col. 4, ll. 43-64 Support in Specification: '159, Col. 6, ll.34-46	**A method to monitor the ability of a promoter to promote expression in an animal of an endogenous gene that is controlled by said promoter:** This phrase should be given its plain and ordinary meaning and no construction is required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart.

Claim Language: '159 Patent	Agreed Proposed Claim Construction	AntiCancer's Proposed Construction	Defendants' Proposed Construction
		"Endogenous gene": a gene normally found within the organism being studied; originating or produced within the organism or one of its parts. Any gene in the animal is endogenous whether original or artificially inserted. Support in Specification: '159, Col. 13, l. 46 to Col. 14. l.9 '159, Col. 15, l. 63 to Col. 16, l. 25 Other Support: Stedman's Medical Dictionary for the Health Professions and Nursing (6th ed.) 507	**"Endogenous gene":** A gene originating within the organism. Support in Specification: Specification at Col. 13, ln. 37 – Col. 14, ln. 3 Extrinsic support: A Dictionary of Genetics 5th Ed. at 113 (definition of endogenous "originating within the organism.")
	"Promoter of said endogenous gene": a promoter associated with a gene that is endogenous to the animal rather than an artificially employed promoter such as a viral promoter (e.g., a CMV promoter) **"Animal"**: a multi-cellular organism of the kingdom of Animalia, characterized by a capacity for locomotion, nonphotosynthetic metabolism, pronounced response to stimuli, restricted growth and fixed bodily structure.		

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	"Expression": a gene is "expressed" when the information encoded in the gene is manifested into an observable characteristic, most commonly the production of a protein.		
a) delivering, to an animal, cells containing a nucleic acid encoding a fluorophore operatively linked to the promoter of said endogenous gene whose ability to promote expression is to be analyzed; and	**"Nucleic Acid"**: DNA or RNA. **"Fluorophore"**: a protein that is auto-fluorescent such that no substrates or co-factors are needed for it to fluoresce. **"operatively linked to the promoter of said endogenous gene whose ability to promote expression is to be analyzed"**: The promoter of the endogenous gene (the gene that is being	**"delivering to an animal, cells containing a nucleic acid encoding a fluorophore"**: giving the animal cells that contain the coding region of a gene, that is a piece of DNA, that can be expressed to produce a fluorophore. Support in Specification: '159 Col. 13, ll. 38-45	**"delivering, to an animal, cells containing a nucleic acid encoding a fluorophore"**: a process in which the nucleic acid is either administered directly into the body of the animal, or the nucleic acid is administered into a cell first, and then the cell containing the nucleic acid is administered into the body of the animal. Support in Specification: Specification at Col. 5, lns. 48-59

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	studied in the method) is linked to and controls the expression of the segment of DNA that contains the code to produce the fluorophore. **"Operatively Linked"**: the functional relationship of DNA with regulatory and effector sequences of nucleotides, such as promoters, enhancers, transcriptional and translational stop sites, and other signal sequences. For example, operative linkage of DNA to a promoter refers to the physical and functional relationship between the DNA and the promoter such that the transcription of such DNA is initiated from the promoter by an RNA polymerase that specifically recognizes, binds to, and transcribes the DNA. **"Fluorescence"**: Emission of a longer wavelength radiation by a substance as a consequence of absorption of energy from a shorter wavelength radiation, continuing only as long as the stimulus is present; distinguished from phosphorescence, which emission persists for a perceptible period of time after the stimulus has been removed.		

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b) observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said animal by whole-body external fluorescent optical imaging, whereby the ability of said promoter to promote expression is monitored, and wherein said fluorophore is a protein that is autofluorescent such that no substrates or cofactors are needed for it to fluoresce.		**"observing the presence, or absence or intensity of the fluorescence generated by said fluorophore at various locations in said animal by whole-body external fluorescent optical imaging:"** observing various locations in the animal to see whether the fluorescence generated by the fluorophore is present or absent, or to observe the intensity of such fluorescence, by a method called whole-body external fluorescent optical imaging. Support in Specification: '159, Col. 5, l. 60 to Col. 6, l. 6 '159, Col. 2, ll. 46-54 **"whole-body external fluorescent optical imaging:"** An imaging process in which the presence, absence or intensity of the fluorescence generated by the fluorophore at various locations in the host organism is monitored, recorded and/or analyzed externally, in real time and on a continuous basis, without any procedure, e.g., surgical procedure, to expose and/or excise the desired observing site from the host organism Support in Specification:	**"observing the presence, or absence or intensity of the fluorescence generated by said fluorophore at various locations in said animal by whole-body external fluorescent optical imaging:"** This phrase should be given its plain and ordinary meaning and no construction is required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart. **"whole-body fluorescent optical imaging":** An imaging process in which the presence, absence, extent or intensity of the fluorescence generated by the fluorophore at various locations in a host organism is monitored, recorded and/or analyzed externally without any procedure (e.g., surgery) to expose and/or to excise the desired observing site from the host organism. Support in Specification: Specification at Col. 5, ln. 60 – Col. 6, ln. 14

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	"whereby the ability of said promoter to promote expression is monitored": whereby the ability of the promoter to cause its associated fluorophore to produce a protein is monitored. **"wherein said fluorophore is a protein that is autofluorescent such that no substrates or cofactors are needed for it to fluoresce"**: wherein the fluorophore is auto-fluorescent such that no other substrates or co-factors are needed for it to fluoresce.	'159, Col. 5, l. 60 to Col. 6, l. 6 '159, Col. 2, ll. 46-54	
5. The method of claim 1, wherein the fluorophore is selected from the group consisting of a green fluorescent protein (GFP), a blue fluorescent protein (BFP) and a red fluorescent protein (RFP).	**"The method of claim 1, wherein the fluorophore is selected from the group consisting of a green fluorescent protein (GFP), a blue fluorescent protein (BFP) and a red fluorescent protein (RFP)":** The method of claim 1, wherein the promoter-linked fluorophore-expressing nucleic acid expresses a fluorophore is either a green fluorescent protein, a blue fluorescent protein, or a red fluorescent protein, except as		

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	to the terms disputed above with respect to independent claim 1.		
7. The method of claim 1, wherein the animal is a mammal.	**"The method of claim 1, wherein the animal is a mammal":** No construction necessary, except as to the terms disputed above with respect to independent claim 1.		
8. The method of claim 7, wherein the mammal is selected from the group consisting of a mouse, a rat, a rabbit, a cat, a dog, a pig, a cow, an ox, a sheep, a goat, a horse, a monkey and a non-human primate.	**"The method of claim 7, wherein the mammal is selected from the group consisting of a mouse, a rat, a rabbit, a cat, a dog, a pig, a cow, an ox, a sheep, a goat, a horse, a monkey and a non-human primate:** No construction necessary, except as to the terms disputed above with respect to independent claim 1.		
9. The method of claim 1, wherein the endogenous gene is normally expressed in a tissue or organ specific manner.		**"The method of claim 1, wherein the endogenous gene is normally expressed in a tissue or organ specific manner":** the method of claim 1, wherein the endogenous gene normally has an expression pattern in which a gene is expressed, either transiently at various levels or constitutively, only in certain tissues or organs, but not in other tissues or organs Support in Specification:	**"The method of claim 1, wherein the endogenous gene is normally expressed in a tissue or organ specific manner":** the method of claim 1, wherein the endogenous gene normally has an expression pattern in which a gene is expressed, either transiently or constitutively, only in certain tissues or organs, but not in other tissues or organs, wherein the construction of endogenous gene is as proposed by Defendants as set forth below.

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		'159 Col. 3, ll. 31-42 '159 Col. 7, ll. 26-38	**"Endogenous gene":** A gene originating within the organism. Support in Specification: '159 Col. 3, lns. 31-42 '159 Col. 7, lns. 26-38 '159 Col. 13, ln. 37 – Col. 14, ln. 3 Extrinsic support: A Dictionary of Genetics 5th Ed. at 113 (definition of endogenous "originating within the organism.")
10. The method of claim 9, wherein the tissue is selected from the group consisting of connective, epithelium, muscle and nerve tissues.	**"The method of claim 9, wherein the tissue is selected from the group consisting of connective, epithelium, muscle and nerve tissues:** No construction necessary, except as to the terms disputed above with respect to independent claims 1 and 9.		

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11. The method of claim 9, wherein the organ is selected from the group consisting of brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, gland, and internal blood vessels.	**11. The method of claim 9, wherein the organ is selected from the group consisting of brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, gland, and internal blood vessels:** No construction necessary, except as to the terms disputed above with respect to independent claims 1 and 9.		

U.S. Patent No. 6,759,038

Claim Language: '038 Patent	Agreed Proposed Claim Construction	AntiCancer's Proposed Construction	Defendants' Proposed Construction
1. A method to evaluate a candidate protocol or drug for the inhibition of metastasis of a primary tumor which method comprises:	**A method to evaluate a candidate protocol or drug for the inhibition of metastasis of a primary tumor which method comprises:** a method to assess the effectiveness of a chosen drug or therapy regimen to reduce the spread of cancer from the primary tumor (the initial growth of cancer). **"Candidate Protocol":** proposed therapy regimen.	**"Metastasis":** the progression, spread, and migration of cancer over time from its initial or primary tumor site via various routes to another part of the body, and/or growth of secondary tumors at that other part of the body. Support: in Specification: '038, Col. 1, ll. 24-64, Col. 3, ll. 5-17, and ll. 60-64, Col. 4, ll.1-5 Extrinsic Support: Stedman's Medical Dictionary for the Health Professions and Nursing 979 (6th ed. 2008); Merriam-Webster's Collegiate Dictionary 780 (11th ed. 2004). (definitions of '**metastasis**')	**"Metastasis":** The growth of secondary tumors from the primary tumor at sites different from the primary tumor. Support in Specification: '038, Col. 1, lns. 24-26; col. 3, lns. 5-8 Extrinsic support: Merriam Webster's Collegiate Dictionary 10th Ed. at 730 (definition of metastasis: "a secondary metastatic growth of a malignant tumor")

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	"Primary Tumor": the original implanted tumor or the first arising tumor.		
administering said protocol or drug to a subject which is a mouse, rat or rabbit which contains a primary tumor that stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes		**"administering said protocol or drug to a subject which is a mouse, rat or rabbit which contains a primary tumor that stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** giving the drug or therapy regimen to a first mouse, rat or rabbit which has a primary tumor that stably and consistently produces green fluorescent protein both in the primary tumor and in the spreading cancer cells/tumors at sites different from the primary tumor. Support in Specification: '038, Col. 3, ll. 26-37 '038, Col. 3, ll. 57-64 **"A primary tumor that stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** A primary tumor whose cells and whose daughter cells maintain the expression of	**"administering said protocol or drug to a subject which is a mouse, rat or rabbit which contains a primary tumor that stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** Giving the drug or protocol to a mouse, rat or rabbit which has a primary tumor that stably produces green fluorescent protein both in the primary tumor and in the spreading cancer cells/tumors at sites different from the primary tumor. Support in Specification: '038, Col. 1, lns. 24-26; '038, Col. 3, lns. 5-22 '038, Col. 3, lns. 26-37 '038, Col. 3, lns. 57-64 '038, Col. 4, lns. 1-10 '038, Col. 5, lns. 16-34 '038, Col. 5, lns. 41-46 **"A primary tumor that stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** This phrase should be given its plain and ordinary meaning and no construction is

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		GFP during metastasis. Support in Specification: '038, Col. 3, ll. 26-37 '038, Col. 3, ll. 57-64 Other Support: Stedman's Medical Dictionary for the Health Professions and Nursing (6th ed.) 551	required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart.
			"stably expresses": the tumor includes cells that consistently express a phenotype, such as GFP, when the cell line proliferates through multiple passages of the cell line, including *in vivo*. Support in Specification and claims: '038, Col. 2, lns. 39-45, '038, Col. 3, lns. 38-44, claim 4, claim 8
		"Green Fluorescent Protein (GFP)": a protein that emits light upon incidence of an excitation; includes any suitable and convenient form of GFP; includes the native gene encoding GFP from Aequorea victoria; includes mutants both naturally and artificially induced, found useful to enhance expression and to modify excitation and fluorescence; includes various forms of GFP including those which exhibit green color and	**"green fluorescent protein (GFP)":** A protein that fluoresces green in its natural state when excited by the appropriate input light ("native GFP"); and man-made fluorescent proteins created by modifying the genetic sequence of a native GFP Support in Specification Specification at Col. 2, lns. 1-2 Specification at Col. 4, lns. 11-48 and citations therein

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		colors other than green; includes but is not limited to GFP which have been isolated from other organisms, such as Renilla reriformis. Support: in Specification: '038, Col. 4, ll. 11-48	Support in Prosecution History: '523 Prosecution, 8/31/98 Office Action (*see* particularly p. 4) Citations in Specification section on GFP: Morin, J. *et al.*, *J Cell l'hystol* (1972) 77:313-318; Prasher, D.C. *et al.*, *Gene* (1992) 111:229-233; Yang, F. *et al.*, *Nature Biotechnol* (1996) 14:1252-1256; Cody, C.W. *et al.*, *Biochemistry* (1993) 32:1212-1218; Heim, R. *et al.*, *Nature* (1995) 373:663-664; U.S. Pat. No. 5,625,048; Delagrave, S. *et al.*, *Biotechnology* (1995) 13:151-154; Cormack, B. *et al.*, *Gene* (1996) 173:33-38; Crameri, A. *et al.*, *Nature Biotechnol* (1996) 14:315-319. Extrinsic Support: Palm, G.J., *et al.*, *"The structural basis for spectral variations in green fluorescent protein,"* 4(5) Nature Structural Biology 361-365 (1997); Patterson, G.H., *et al.*, *"Use of Green Fluorescent Protein and Its Mutants in Quantitative Fluorescence Microscopy,"* 73 Biophysical Journal 2782-2790 (1997); Cormack, B.P., *et al.*, *"FAC'S-optimized mutants of the green fluorescent protein (GFP),"* 173 Gene 33-38 (1996); Heim, R., *et al.*, *"Improved green*

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			fluorescence," 373(6516) Nature 663-664 (1995); Crameri, A., *et al.*, *"Improved Green Fluorescent Protein by Molecular Evolution Using DNA Shuffling"* 14 Nature Biotechnology 315-319 (1996); Delagrave, S., *et al.*, *"Red-Shifted Excitation Mutants of the Green Fluorescent Protein,"* 13(2) Biotechnology 151-154 (1995); Prasher, D.C., *"Using GFP to see the light," 11(8)* TIG 320-323 (1995); Prasher, D.C., *et al.*, *"Primary structure of the Aeqziorea victoria green-fluorescent protein,"* 111 Gene 229-233 (1992); Yang, F., *et al.*, *"The molecular structure of green fluorescent protein,"* 14 Nature Biotechnology 1246-1251 (1996); Chalfie, M., *et al.*, *"Green Fluorescent Protein as a Marker for Gene Expression,"* 263(5148) Science 802-805 (1994); Yang, M., *et al.*, *"Whole-body optical imaging of green fluorescent protein-expressing tumors and metastases,"* 97(3) PNAS 1206-1211 (2000); Plautz, J., et al., "Green fluorescent protein and its derivatives as versatile markers for gene expression in living Drosophila melanogaster, plant and mammalian cells." 173 Gene 83-87 (1996).

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		"metastasize": to progress, spread, and migrate cancer over time from its initial or primary tumor site via various routes to another part of the body, and/or growth of secondary tumors at that other part of the body. Support: in Specification: '038, Col. 1, ll. 24-64, Col. 3, ll. 5-17, and ll. 60-64, Col. 4, ll.1-5 Extrinsic Support: Stedman's Medical Dictionary for the Health Professions and Nursing 979 (6th ed. 2008); Merriam-Webster's Collegiate Dictionary 780 (11th ed. 2004). (definitions of '**metastasis**')	**metastasize:** to form secondary tumors from the primary tumor at sites different from the primary tumor. Support in Specification: '038, Col. 1, lns. 24-26; col. 3, lns. 5-8 Extrinsic support: Merriam Webster's Collegiate Dictionary 10th Ed. at 730 (definition of metastasis: "a secondary metastatic growth of a malignant tumor")
and monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence at various locations in the treated subject;		**"and monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence at various locations in the treated subject":** Monitoring in a subject the spread of cancer to sites different from the primary tumor by observing various locations in the animal to see whether the fluorescence is present or absent, or to observe the intensity of such fluorescence. Support in Specification: '038, Col. 3, ll. 6-22	**"and monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence at various locations in the treated subject":** This phrase should be given its plain and ordinary meaning and no construction is required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart. Were the Court to construe the term, the term should be construed according to its plain meaning as monitoring in a subject the spread of cancer to sites

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	"Fluorescence": Emission of a longer wavelength light by a substance when it is being excited by shorter wavelength light (such as, e.g., the emission of green light by GFP when excited by blue or ultraviolet light), where the light emission continues only as long as the exciting light is shining on the substance.	'038, Col. 5, ll. 28-34 '038, Col. 1, ll. 25-37 '038, Col. 4, ll. 1-10 '038, Col. 5, ll. 23-28 '038, Col. 5, ll. 41-46	different from the primary tumor to see whether the fluorescence is present or absent, or to observe the intensity of such fluorescence. Support in Specification: '038, Col. 1, lns. 24-26 '038, Col. 3, lns. 5-22 '038, Col. 4, lns. 1-10 '038, Col. 5, lns. 16-34 '038, Col. 5, lns. 41-46 Extrinsic support: Merriam Webster's Collegiate Dictionary 10th Ed. at 730 (definition of metastasis: "a secondary metastatic growth of a malignant tumor")
wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat or rabbit, or a mouse, rat		**"wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat**	**"wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat or rabbit, or a mouse,**

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or rabbit which is syngeneic to said tumor;		**or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor":** Wherein the subject contains a tumor that produces GFP, and wherein the subject is a mouse, rat, or rabbit that have impaired immune systems; denoting an individual whose immunologic mechanism is deficient, or alternatively, the tumor is derived from a genetically compatible source to the mouse, rat or rabbit that are immunocompetent. Support in Specification: '038, Col. 3, ll. 26-29 '038, Col. 5, l. 60 to Col. 6 l. 2 **"Genetically Immunocompromised":** Having an inherited genetic defect which causes the subject's immune system to be deficient or impaired (such as nude and SCID mice). Support in Specification: '038, Col. 3, ll. 26-29 '038, Col. 5, l. 60 to Col. 6 l. 2	**rat or rabbit which is syngeneic to said tumor":** Wherein the subject contains a tumor that expresses GFP, and wherein the subject is a mouse, rat or rabbit that has a deficient immune system caused by an inherited genetic defect; or alternatively, the tumor is derived from a generically identical source to the control mouse, rat or rabbit. Support in '038 Prosecution History: 5/29/01 Preliminary Amendment (*see* 11/18/02 Amendment (*see* particularly at p. 4-5); Declaration of Hoffman (*see* particularly p 4) 3/12/03 Office Action (*see* particularly pp. 3-5); 6/18/02 Office Action 6/12/03 Amendment (*see* particularly at p. 2-3 & 5) **"genetically immunocompromised":** A deficient immune system caused by an inherited genetic defect; does not cover a subject which is immunocompromised by irradiation or by providing immunosuppressants. Support in '038 Prosecution History:

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	"Syngeneic": Genetically identical; includes a tumor derived from the same mouse.		5/29/01 Preliminary Amendment (*see* 11/18/02 Amendment (*see* particularly at p. 4-5); Declaration of Hoffman (*see* particularly p 4) 3/12/03 Office Action (*see* particularly pp. 3-5); 6/18/02 Office Action 6/12/03 Amendment (*see* particularly at p. 2-3 & 5)
monitoring the progression of metastasis in a control, which contains a similar tumor that expresses green fluorescent protein;		**"monitoring the progression of metastasis in a control, which contains a similar tumor that expresses green fluorescent protein":** in a control animal (an animal that is not administered the chosen drug or therapy) which contains a tumor that is similar to the one given the treated animal and produces GFP, monitoring the spread of cancer. Support in Specification: '038, Col. 3, ll. 6-11 '038, Col. 4, ll. 1-7 '038, Col. 5, ll. 25-28	**"monitoring the progression of metastasis in a control, which contains a similar tumor that expresses green fluorescent protein":** monitoring the progression of metastasis in a control, which can be the same animal but with respect to a "similar (but distinct) tumor" in that same animal, where that similar tumor expresses green fluorescent protein. Support in Specification: '038, Col. 4, lns. 7-10 '038, Col. 13, lns. 51-56 Extrinsic support: Dorland's Illustrated Medical Dictionary 27th Ed. at 376

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			(definition 2 of control "a standard against which experimental observations may be evaluated, as a procedure identical in all respects to the experimental procedure except for absence of the one factor that is being studied.")
wherein said control subject contains said tumor that expresses GFP wherein said control subject is an immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor;		**"wherein said control subject contains said tumor that expresses GFP wherein said control subject is an immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor":** wherein the control contains a tumor that expresses GFP, and wherein the control subjects have an impaired immune systems; denoting an individual whose immunologic mechanism is deficient, or alternatively, the tumor is derived from a genetically compatible source to the control mouse, rat or rabbit that are immunocompetent. Support in Specification: '038, Col. 3, ll. 26-29 '038, Col. 5, l. 60 to Col. 6 l. 2	**"wherein said control subject contains said tumor that expresses GFP wherein said control subject is an immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor":** wherein the control, which can be the same animal but with respect to a "similar (but distinct) tumor" in that same animal, where that similar tumor expresses green fluorescent protein, and wherein the control subject is a mouse, rat or rabbit that has a deficient immune system caused by an inherited genetic defect; or alternatively, the tumor is derived from a genetically identical source to the control mouse, rat or rabbit. Support in Specification: '038, Col. 4, lns. 7-10 '038, Col. 13, lns. 51-56 Support in claim language: '038, Col. 14, lns. 1-4

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			Support in '038 Prosecution History: 5/29/01 Preliminary Amendment (*see* 11/18/02 Amendment (*see* particularly at p. 4-5); Declaration of Hoffman (*see* particularly p 4) 3/12/03 Office Action (*see* particularly pp. 3-5); 6/18/02 Office Action 6/12/03 Amendment (*see* particularly at p. 2-3 & 5) Extrinsic support: Dorland's Illustrated Medical Dictionary 27th Ed. at 376 (definition 2 of control "a standard against which experimental observations may be evaluated, as a procedure identical in all respects to the experimental procedure except for absence of the one factor that is being studied.")
and comparing the progression of metastasis in said treated subject with the progression of metastasis in said control subject wherein the control subject and treated subject are intact;		**"comparing the progression of metastasis in said treated subject with the progression of metastasis in said control subject wherein the control subject and treated subject are intact":** comparing the spread of cancer from the primary tumor in the treated intact mouse, rat or	**"comparing the progression of metastasis in said treated subject with the progression of metastasis in said control subject wherein the control subject and treated subject are intact":** comparing the spread of cancer from the primary tumor in the intact treated mouse, rat or

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		rabbit (the one that received the chosen drug or therapy) as compared to the control intact mouse, rat or rabbit (the one that did not receive the chosen drug or therapy). Support in Specification: '038, Col. 5, ll. 32-36 '038, Col. 5, ll. 42-55 '038, Col. 13, ll. 51-56	rabbit as compared to the control intact mouse, rat or rabbit, which can be the same animal but with respect to a "similar (but distinct) tumor" in that same animal. Support in Specification: '038, Col. 4, lns. 7-10 '038, Col. 13, lns. 51-56 '038, Col. 5, lns. 27-36 Extrinsic support: Dorland's Illustrated Medical Dictionary 27th Ed. at 376 (definition 2 of control "a standard against which experimental observations may be evaluated, as a procedure identical in all respects to the experimental procedure except for absence of the one factor that is being studied.")
		"intact subject": a subject without any surgical openings in the skin. Support in Specification: '038, Col. 5, ll. 3 1-33	**"intact"**: of a living body or its parts: having no relevant component removed or destroyed. Support in Specification: '038, Col. 5, lns. 24-36 '038, Col. 12, lns. 13-16 '038, Col. 12, lns. 26-32 Extrinsic support: Merriam Webster's Collegiate Dictionary 10th Ed. at 607 (definition 2 of intact: "of a

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			living body or its parts: having no relevant component removed or destroyed.")
whereby a diminution of the progression of metastasis in said treated subject as compared to said control subject identifies the protocol or drug as effective in inhibiting metastasis.		**"whereby a diminution of the progression of metastasis in said treated subject as compared to said control subject identifies the protocol or drug as effective in inhibiting metastasis":** Inhibition of metastasis by the proposed treatment or drug is identified as lower levels of fluorescence emitted by GFP-expressing tumor cells at primary and distal sites in intact subjects treated with the drug or proposed treatment in comparison to the levels of fluorescence emitted by GFP-expressing tumor cells at primary and distal sites in intact subjects untreated with the drug or proposed treatment. Support in Specification: '038, Col. 5, ll. 42-55 '038, Col. 13, ll. 51-56	**"whereby a diminution of the progression of metastasis in said treated subject as compared to said control subject identifies the protocol or drug as effective in inhibiting metastasis":** The protocol or drug effective in inhibition of metastasis can be identified as lower levels of fluorescence emitted by GFP-expressing tumor cells in the primary tumor and in the spreading cancer cells/tumors in the treated subject as compared to the control mouse, rat or rabbit, which can be the same animal but with respect to a "similar (but distinct) tumor" in that same animal. Support in Specification: '038, Col. 4, lns. 7-10 '038, Col. 13, lns. 51-56 '038, Col. 3, lns. 6-22 '038, Col. 4, lns. 1-10 '038, Col. 5, lns. 16-34 '038, Col. 5, lns. 41-46 Extrinsic support: Dorland's Illustrated Medical Dictionary 27th Ed. at 376

Claim Language: '038 Patent	Agreed Proposed Claim Construction	AntiCancer's Proposed Construction	Defendants' Proposed Construction
			(definition 2 of control "a standard against which experimental observations may be evaluated, as a procedure identical in all respects to the experimental procedure except for absence of the one factor that is being studied.")
2. The method of claim 1 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject.		**"The method of claim 1 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject":** The method of claim 1, wherein the spread of cancer from the primary tumor is observed in an intact subject by causing the tumor to fluoresce and observing such fluorescence. **"Fluorescent optical tumor imaging":** Acquiring a light image of a fluorescent tumor or fluorescent tumor cells of a subject. Support in Specification: '038, Col 3, ll. 19-22 '038, Col. 5, ll. 42-55	**"The method of claim 1 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject":** This phrase should be given its plain and ordinary meaning and no construction is required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart with respect to independent claim 1 and as set forth below. **"intact subject"**: *see above* **"Fluorescent optical tumor imaging"**:The use of fluorescence for real-time observation and monitoring the progression of metastasis on a continuous basis. Support in Specification: Specification at Col. 5, lns. 41-45 Specification at Col. 3, lns. 9-18 Specification at Col. 12, ln. 60 - Col.13, ln. 5

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			Support in '038 Prosecution: Preliminary Amendment of May 29, 2001 at p. 5 Support in '384 Prosecution Application at pp. 23-24 8/30/99 Office Action (*see* particularly p. 8-12) 11/16/99 Interview Summary 11/23/99 Interview Summary 2/29/00 Amendment (*see* particularly pp. 1, 2 and 5) 6/21/00 Office Action (*see* particularly p. 6-7); Decl. of Hoffman (*see* particularly p. 5 & articles cited therein)
5. A method to monitor metastasis of a primary tumor in a subject which is a mouse, rat or rabbit which contains said primary tumor, and wherein said tumor stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes,		**"A method to monitor metastasis of a primary tumor in a subject which is a mouse, rat or rabbit which contains said primary tumor, and wherein said tumor stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** A method to monitor the spread of cancer from a primary tumor in a mouse, rat or rabbit, which has a primary tumor that stably and consistently produces green fluorescent protein both in the primary tumor and in the spreading cancer cells/tumors.	**"A method to monitor metastasis of a primary tumor in a subject which is a mouse, rat or rabbit which contains said primary tumor, and wherein said tumor stably expresses green fluorescent protein (GFP) in cells of said tumor when said tumor metastasizes":** A method to monitor the spread of cancer from a primary tumor in a mouse, rat or rabbit, which has a primary tumor that stably produces green fluorescent protein both in the primary tumor and in the spreading cancer cells/tumors.

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		Support in Specification: '038, Col 1, ll. 24-26 '038, Col. 4, ll. 51-54	Support in Specification: '038, Col. 1, lns. 24-26 '038, Col. 3, lns. 5-22 '038, Col. 4, lns. 1-10 '038, Col. 5, lns. 16-34 '038, Col. 5, lns. 41-46
wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor;		**"wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor":** wherein the subject contains a tumor that produces GFP, and wherein the subject has an impaired immune system, or alternatively, the tumor is derived from a genetically compatible source to the mouse, rat or rabbit with an intact immune system. Support in Specification: '038, Col. 3, ll. 26-29 '038, Col. 5, l. 60 to Col. 6 l. 2	**"wherein said subject contains said tumor that expresses GFP and wherein said subject is a genetically immunocompromised mouse, rat or rabbit, or a mouse, rat or rabbit which is syngeneic to said tumor":** wherein the subject contains a tumor that expresses GFP, and wherein the subject is a mouse, rat or rabbit that has a deficient immune system caused by an inherited genetic defect; or alternatively, the tumor is derived from a genetically identical source to the control mouse, rat or rabbit. Support in Specification: '038, Col. 3, lns. 26-29 '038, Col. 5, ln. 60 to Col. 6, ln.2 Support in '038 Prosecution History: 5/29/01 Preliminary Amendment (*see* 11/18/02 Amendment (*see* particularly at p. 4-5); Declaration of Hoffman (*see* particularly p 4) 3/12/03 Office Action (*see*

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			particularly pp. 3-5); 6/12/03 Amendment (*see* particularly at p. 2-3 & 5)
which method comprises monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence as a function of time at various locations in said subject wherein the subject is intact.		**"which method comprises monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence as a function of time at various locations in said subject wherein the subject is intact":** monitoring in an intact animal the spread of cancer from the primary tumor by observing at various locations in the mammal changes over time in the presence	**"which method comprises monitoring the progression of metastasis by observing the presence, absence or intensity of the fluorescence as a function of time at various locations in said subject wherein the subject is intact":** monitoring in an intact animal the spread of cancer from the primary to sites different from the primary tumor by observing whether the fluorescence is present

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		or absence or intensity of the fluorescence. Support in Specification: '038, Col. 5, ll. 42-55 '038, Col. 13, ll. 5 1-56	or absent, or by observing the intensity of such fluorescence over time. Support in Specification: '038, Col. 1, lns. 24-26 '038, Col. 3, lns. 5-22 '038, Col. 4, lns. 1-10 '038, Col. 5, lns. 16-34 '038, Col. 5, lns. 41-46
6. The method of claim 5 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject.		**"The method of claim 5 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject":** the method of claim 5, wherein the spread of cancer from the primary tumor is observed in an intact subject by the specific observation technique known as "fluorescent optical tumor imaging." Support in Specification: '038, Col 3, ll. 19-22	**"The method of claim 5 wherein the progression of metastasis is monitored by fluorescent optical tumor imaging in the intact subject":** This phrase should be given its plain and ordinary meaning and no construction is required beyond the constructions for individual terms within the phrase that are proposed by Defendants as set forth in this chart with respect to independent claim 5, and the construction of fluorescent optical imaging as set forth above in claim 2.